

**5.08 BENRALIZUMAB,
Injection 30 mg in 1 mL pre-filled pen,
Fasenra Pen™,
AstraZeneca Pty Ltd.**

1 Purpose of Application

- 1.1 The minor submission sought a Section 100 (Highly Specialised Drugs Program) listing for a new presentation of benralizumab (pre-filled pen/auto-injector form; Fasenra Pen from herein) for the treatment of uncontrolled severe eosinophilic asthma.

2 Background

Previous PBAC consideration

- 2.1 Benralizumab (pre-filled syringe; Fasenra PFS from herein) was first considered by the PBAC at its March 2018 meeting and was recommended by the PBAC on a cost-minimisation basis to mepolizumab. Fasenra PFS was PBS-listed in December 2018.

Registration status

- 2.2 Fasenra Pen was TGA registered on 10 December 2019 with the same indication as Fasenra PFS.
- 2.3 The TGA delegate considered that exposure to both Fasenra Pen and Fasenra PFS to be the same. The TGA Delegate noted that Fasenra PFS and pen used in the clinical studies were not identical to the products proposed for marketing in Australia, however these changes were not considered to be important in the usability or functionality of the device.

3 Requested listing

- 3.1 The submission requested the listing of Fasenra Pen under the same conditions as the currently PBS-listed Fasenra PFS.
- 3.2 The pre-PBAC response noted the PBAC's long-standing position to not recommend pharmacy-level substitution ('a'-flagging) for devices with different injecting techniques. However, the pre-PBAC response noted that the sponsor was developing processes to manage concerns about patient education on the correct use of the two different devices to help patients move from Fasenra PFS to Fasenra Pen if pharmacy-level substitution was recommended.

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from 1 organisation via the Consumer Comments facility on the PBS website. Asthma Australia provided comments, which described a range of benefits of having the new pen form available including increasing patient choice between delivery device, and the ease of use of an injection pen compared to the PFS form.

Clinical trials

- 4.3 The minor submission presented one head-to-head study (AMES Clinical Study Report (CSR)) comparing the delivery of Fasenra Pen and PFS.
- 4.4 AMES was a multicentre, randomised, 8-week, open-label, parallel group, Phase 1 study measuring the exposure of Fasenra Pen and PFS in 180 healthy patients. The study's primary objective was to compare the pharmacokinetic (PK) effects between the two presentations. The secondary objectives of the study also included measuring the PK effects in different injection sites and in patients with different body weights; and evaluating the safety, tolerability and immunogenicity.
- 4.5 The minor submission presented no bioequivalence studies comparing Fasenra Pen and PFS. The submission noted that although the pen and PFS were different devices, both contain the same biological medicine and therefore a bioequivalence study was not a requirement for TGA registration.

Comparative effectiveness

- 4.6 The results of the AMES study demonstrated that the PK measurements following injection of either Fasenra Pen or PFS, were within the acceptable reference ranges.

Therefore, the primary objectives of the study to find comparability between the presentations were met:

- Geometric mean ratios (pen/PFS) for AUC_{last} , AUC_{inf} , and C_{max} were 92.83%, 94.46%, and 92.34% respectively.
- The 90% confidence intervals for all three parameters were within the 80-125% range determined for claiming equivalence.

Comparative harms

- 4.7 The AMES study recorded that 96 patients reported at least 1 adverse event (53.3% of the whole cohort). The most commonly reported adverse event included nasopharyngitis, headache and oropharyngeal pain. The number of adverse events were similar between the PFS (51.1%) and pen (55.6%). There were no deaths, serious adverse events, or new safety findings recorded in the study. It was noted in the CSR that there was a higher rate of headaches when using the pen form (15.6%) compared with the PFS (5.6%). The pre-PBAC response considered that as three patients in each trial arm experienced headaches that were linked to treatment; this indicated there was no difference in the incidence of headaches between Fasenra Pen and PFS.

For more detail on PBAC's view, see section 5 PBAC outcome.

Clinical claim

- 4.8 The minor submission claimed that Fasenra Pen and PFS contain the same formulation and are therefore equivalent.
- 4.9 The PBAC considered that the claim of equivalent comparative effectiveness and comparative safety was reasonable.

For more detail on PBAC's view, see section 5 PBAC outcome.

Economic analysis

- 4.10 The minor submission presented a cost-minimisation analysis of Fasenra Pen compared with Fasenra PFS. The proposed equi-effective doses were one benralizumab 30 mg in 1 mL pen is equivalent to one benralizumab 30 mg in 1 mL PFS.
- 4.11 The submission proposed that the Special Pricing Arrangement for Fasenra PFS should apply for Fasenra Pen.

For more detail on PBAC's view, see section 5 PBAC outcome.

Estimated PBS usage & financial implications

- 4.12 The minor submission did not expect the listing of the pen form to grow the overall benralizumab market or the broader biologic medicines for severe asthma market. However, the submission noted that it is expected that most patients on Fasenra would prefer the pen form and substitution between the two forms would occur.

- 4.13 The minor submission estimated there to be no financial implications to the PBS as a result of listing Fasenra Pen as it is expected the pen will only substitute for the PFS and both presentations will have the same price.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of a new form of benralizumab (pre-filled pen/auto-injector form; Fasenra Pen), on the basis that it should be available only under special arrangements under Section 100 (Highly Specialised Drugs Program) for the treatment of uncontrolled severe eosinophilic asthma.
- 5.2 The PBAC recommended the listing of Fasenra Pen on a cost-minimisation basis to benralizumab (pre-filled syringe; Fasenra PFS), with equi-effective doses being one benralizumab 30 mg in 1 mL Pen equivalent to one benralizumab 30 mg in 1 mL PFS.
- 5.3 The PBAC recommended the restrictions for Fasenra Pen should be consistent with the current restrictions for Fasenra PFS for the treatment of uncontrolled severe eosinophilic asthma.
- 5.4 The PBAC considered that Fasenra Pen was equivalent to Fasenra PFS in terms of comparative efficacy and safety which was supported by the AMES study. It was also noted the TGA Delegate considered the same exposure to both presentations to be the same.
- 5.5 The PBAC considered that there should be no financial implications with the listing of the pen form of benralizumab as the new form would not grow the overall biologics market in severe asthma, but rather substitute for use of the PFS.
- 5.6 The PBAC reaffirmed its March 2018 advice, under Section 101 (3BA) of the *National Health Act 1953*, that benralizumab and mepolizumab should be treated as interchangeable on an individual patient basis (paragraph 7.16, item 5.01 benralizumab, Public Summary Document (PSD), March 2018, PBAC meeting).
- 5.7 The PBAC advised, under Section 101 (4AACD) of the *National Health Act 1953*, that benralizumab 30 mg/mL injection, 1 mL pen device and benralizumab 30 mg/mL injection, 1 mL syringe should not be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS of one form and PBS of another form are equivalent for the purposes of substitution at the pharmacy level). The PBAC noted the two forms had different injection techniques and there was a risk of incorrect injecting of a dose if patients are dispensed a different presentation to what they were trained to use.
- 5.8 The PBAC advised that benralizumab is not suitable for prescribing by nurse practitioners.
- 5.9 The PBAC recommended that the Early Supply Rule should not apply.

5.10 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Add new items:

Name, Restriction, Manner of administration and form	PBS item code	Max. Qty packs	Max. Qty units	No. of Rpts	Proprietary Name and Manufacturer	
BENRALIZUMAB benralizumab 30 mg/mL injection, 1 mL pen device	NEW (Private) NEW (Public)	1	1	4	Fasenra Pen™	AstraZeneca Pty Ltd

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

The sponsor had no comment.